

WHAT IS CLAIMED IS:

1. A modified chemokine characterized by truncation of between about 2 to about 8 amino acids at the amino terminus of a mature chemokine and by at least a log higher biological activity than the mature chemokine.

2. The protein according to claim 1 wherein said mature chemokine is selected from the group consisting of KC, gro- β , gro- γ , and gro- α , said chemokines of mammalian origin.

3. The modified chemokine according to claim 1 comprising the amino acid sequence of the mature KC protein having its amino terminus truncated at a position between amino acid residues #2 through 8 of SEQ ID NO: 1, wherein said modified chemokine is characterized by having biological activity.

4. The modified chemokine according to claim 3 consisting essentially of amino acids 5-72 of SEQ ID NO: 1.

5. The modified chemokine according to claim 1 comprising the amino acid sequence of mature gro- β protein truncated at its N terminus between amino acid positions 2 and 8 of SEQ ID NO: 3.

6. The modified chemokine according to claim 5 consisting essentially of amino acids 5 to 73 of SEQ ID NO: 3.

7. The modified chemokine according to claim 1 comprising the amino acid sequence of mature gro- α protein truncated at its N terminus between amino acid positions 2 and 8 of SEQ ID NO: 2.

8. The modified chemokine according to claim 7 consisting essentially of amino acids 5 to 73 of SEQ ID NO: 2.

9. The modified chemokine according to claim 1 comprising the amino acid sequence of mature gro- γ protein truncated at its N terminus between amino acid positions 2 and 8 of SEQ ID NO: 4.

10. The modified chemokine according to claim 9 consisting essentially of amino acids 5 to 73 of SEQ ID NO: 4.

11. A modified chemokine which is characterized by truncation of between about two to about 8 amino acids at the carboxy terminus of the mature chemokine and by at least a log higher biological activity than the mature chemokine.

12. The modified chemokine according to claim 11 comprising the amino acid sequence of the mature KC protein having its carboxy terminus truncated at a position between amino acid residues #58 through 70 of SEQ ID NO: 1, wherein said modified KC is characterized by having biological activity.

13. The modified chemokine according to claim 12 consisting essentially of amino acids 1 to 68 of SEQ ID NO: 1.

14. A multimeric protein which comprises an association of one or more modified chemokines selected from the group consisting of

(a) a modified chemokine characterized by truncation of between about 2 to about 8 amino acids at the amino terminus of the mature chemokine and by at least a log greater biological activity than that of the mature chemokine; and

(b) a modified chemokine which is characterized by truncation of between about 2 to about 10 amino acids at the carboxy terminus of the mature chemokine and by at least a log greater biological activity than that of the mature chemokine.

15. The protein according to claim 14 comprising multiple copies of the same modified chemokine.

16. The protein according to claim 14 comprising at least two different modified chemokines.

17. The protein according to claim 14 wherein said second chemokine comprises a mature chemokine.

18. A nucleic acid sequence comprising the sequence encoding a modified chemokine selected from the group consisting of

(a) a modified chemokine characterized by truncation of between about 2 to about 8 amino acids at the amino terminus of the mature protein and by at least the biological activity of the mature protein;

(b) a modified chemokine which is characterized by truncation of between about 2 to about 10 amino acids at the carboxy terminus of the mature protein and by at least the biological activity of the mature protein; and

(c) a multimeric protein comprising at least one of the proteins (a) or (b), optionally in association with a second chemokine.

19. A plasmid comprising the nucleic acid sequence according to claim 18 under the control of selected regulatory sequences capable of directing the replication and expression thereof in a host cell.

20. A host cell transfected with a plasmid of claim 19.

21. A method of producing a modified chemokine comprising culturing a host cell of claim 20 and isolating the chemokine from the cell or cell culture.

22. A method of enhancing the biological activity of a chemokine by performing at least one of the steps comprising:

(a) removing from the amino terminus of the mature protein about 2 to about 8 of the mature chemokine amino acid residues; and

(b) removing from the carboxy terminus of the mature protein about 2 to about 10 of the mature chemokine amino acid residues.

23. A pharmaceutical composition comprising a modified chemokine selected from the group consisting of

(a) a modified chemokine characterized by truncation of between about two to about 8 amino acids at the amino terminus of the mature protein and by at least a log greater biological activity than that the full-length mature chemokine;

(b) a modified chemokine which is characterized by truncation of between about two to about 10 amino acids at the carboxy terminus of the mature protein and by at least the biological activity of the full-length mature chemokine; and

(c) a multimeric protein comprising at least one of the chemokines (a) or (b) optionally in association with a second chemokine, in a suitable pharmaceutical carrier.

24. A method for treating an inflammatory condition comprising administering to a mammalian subject characterized by said condition an effective amount of a pharmaceutical composition of claim 23.

25. A method of stimulating the growth and/or differentiation of bone marrow cells in a mammal, said improvement comprising: administering to said mammal a modified chemokine according to claim 1 or 11.

26. An improved method of stimulating maturation of hematopoietic precursor cells in a mammal, said improvement comprising administering to said mammal a modified chemokine according to claim 1 or 11.

27. An improved method of stimulating the growth and/or differentiation of bone marrow cells in a mammal, said improvement comprising administering to said mammal a mixture of GM-CSF and a modified chemokine according to claim 1 or 11, wherein said mixture is characterized by having a synergistic effect.

28. An antibody capable of selectively binding to a modified chemokine according to claim 1.

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29. An antibody capable of selectively binding to a modified chemokine according to claim 11.

30. A method for monitoring the circulating level of a selected agent characterized by the ability to induce a hematopoietic synergistic factor in a mammal comprising:

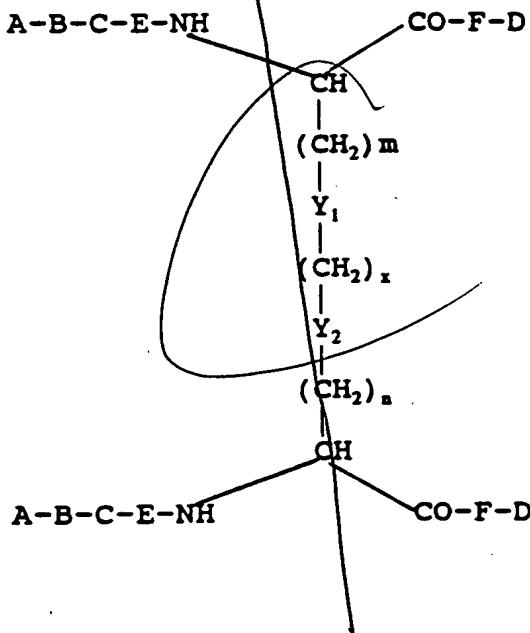
contacting a blood sample from the mammal with an antibody according to claim 28 or 29,

measuring levels of circulating HSF, and

comparing said circulating HSF levels following administration of said agent to circulating HSF levels prior to administration of said agent.

31. The method according to claim 30 wherein said antibody is optionally associated with a detectable label.

32. A method of inducing a hematopoietic synergistic factor in vivo comprising administering to a selected mammal a compound of the following formula:



wherein:

Y_1 and Y_2 are independently CH_2 or S;

x is 0, 1, 2, 3, or 4;

m is 0, 1, or 2;

n is 0, 1, or 2;

A is pyroglutamic acid, proline, glutamine, tyrosine, glutamic acid, 2-thiophene carboxylic acid, picolinic acid, cyclohexane carboxylic acid, tetrahydro-2-furoic acid, tetrahydro-3-furoic acid, 2-oxo-4-thiazolidine, cyclopentane, 3-thiophene carboxylic acid, 5-oxo-2-tetrahydrofuran carboxylic acid, and pipercolinic acid;

B is serine, glutamic acid, tyrosine or aspartic acid;

C is glutamic acid, tyrosine or aspartic acid;

D is lysine, arginine, tyrosine, N-methylarginine, aspartic acid, ornithine or diaminohexanoic acid; or the carboxyamide, or hydroxy methyl derivative thereof;

E is glutamic acid, aspartic acid, tyrosine or a peptide bond;

F is tyrosine or a peptide bond;

provided that:

when Y_1 and Y_2 are S, x is 2, 3 or 4 and m and n are 1; or

when Y_1 and Y_2 are CH_2 , x is 0, 1 or 2 and m and n are 0;

or

when Y_1 is S and Y_2 is CH_2 , x is 0 and n is 1; or

when Y_2 is S and Y_1 is CH_2 , x is 0 and m is 1; or a pharmaceutically acceptable salt thereof.

33. The method according to claim 32 wherein the peptide is selected from the group consisting of:

(pGlu-Glu-Asp),₂Sub(Lys), SEQ ID NO: 5

(pGlu-Glu-Asp),₂Adp(Lys), SEQ ID NO: 6

(pGlu-Glu-Glu),₂Sub(Lys), SEQ ID NO: 7

(pGlu-Asp-Asp),₂Sub(Lys), SEQ ID NO: 8

(Pic-Glu-Asp),₂Sub(Lys), SEQ ID NO: 9

~~(L-Ppc-Glu-Asp),₂Sub(Lys),₂ SEQ ID NO: 10~~
~~(pGlu-Ser-Asp),₂Sub(Lys),₂ SEQ ID NO: 11~~
~~(pGlu-Ser-Asp),₂Akp(Lys),₂ SEQ ID NO: 12~~
~~(pGlu-Ser-Asp),₂Akp(Lys-NH₂),₂ SEQ ID NO: 13~~
~~(Pic-Ser-Asp),₂Akp(Lys),₂ SEQ ID NO: 14~~
~~(Pic-Ser-Asp),₂Akp(Lys-NH₂),₂ SEQ ID NO: 15~~
~~(pGlu-Glu-Asp),₂Akp(Tyr-Lys),₂ SEQ ID NO: 16~~
~~(Pic-Glu-Asp),₂Akp(Lys),₂ SEQ ID NO: 17~~
~~(p-Glu-Glu-Asp),₂Sub(Lys-NH₂),₂ SEQ ID NO: 18~~
~~(Pic-Glu-Asp),₂Akp(Lys-NH₂),₂ SEQ ID NO: 19~~

34. The method according to claim 32 wherein said peptide is administered in amounts of between about 0.01 ng/kg to 1 g/kg.

35. The method according to claim 33 wherein the peptide is ~~(pGlu-Glu-Asp),-Sub-(Lys),₂ SEQ ID NO: 5.~~

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